Pitfalls of Technetium-99m (Tc99m) Sestamibi scintigraphy for suspected parathyroid adenomas

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Learning objectives

- To demonstrate potential pitfalls of Tc99m Sestamibi scintigraphy for localisation of parathyroid adenomas.
Background

Primary hyperparathyroidism (PHPT) is the third most common endocrine disorder with a prevalence of 1/1,000 [1,2]. It is confirmed by an elevated parathyroid hormone level (PTH) and over 80% of cases are caused by a solitary adenoma [3]. Up to 20% of these solitary adenomas are found in ectopic locations which relate to the aberrant migration of the parathyroid glands during embryological development [2]. Other rarer causes of PHPT include parathyroid hyperplasia [15%], multiple adenomas (3-5%) and parathyroid carcinomas (1%) [3].

The parathyroid glands' key role is regulation of calcium levels in the blood by releasing parathyroid hormone (PTH) [2]. Clinical symptoms of PHPT are usually as a result of hypercalcaemia and include weakness, depression, constipation, polydipsia, polyuria and fatigue [2,3]. Physical manifestations may present as pancreatitis, nephrocalcinosis, renal lithiasis, peptic ulcer disease, osteitis fibrosa cystica and osteoporosis [3].

Surgery is the most effective treatment for symptomatic primary hyperparathyroidism [3]. Tc99m Sestamibi scintigraphy plays an increasingly important role in localising parathyroid adenomas prior to surgery, however radiologists are faced with numerous challenges when trying to accurately interpret these images [1,2].
Findings and procedure details

We present a pictorial review of four cases of primary hyperparathyroidism, demonstrating various pitfalls of using Tc99m Sestamibi to localise parathyroid adenomas.

Case 1: A 74-year old female presented with PHPT and osteoporosis. Blood investigations revealed an adjusted calcium of 2.63 mmol/L, a PTH of 10.7 pmol/L and phosphate of 0.99 mmol/L.

An initial parathyroid Tc99m Sestamibi was performed which showed normal distribution of tracer uptake and no parathyroid adenoma was identified.

Repeat imaging was requested 8 months later due to a deterioration in bone density and continued primary hyperparathyroidism. This demonstrated asymmetrical tracer accumulation in the submandibular glands with increased uptake seen on the left; thought to represent either physiological uptake or an ectopic parathyroid adenoma (Figure 1).

A neck ultrasound was performed for further evaluation, which demonstrated no evidence of a parathyroid adenoma with unremarkable thyroid and submandibular glands.

A CT neck with contrast was subsequently performed (Figures 2). This demonstrated an enhancing 8 x 10 mm nodule seen anterior to the left submandibular gland corresponding to the focal tracer accumulation on the Sestamibi scan.

An USS guided fine needle aspiration (FNA) was subsequently performed.

The histology demonstrated reactive lymphoid tissue.

Learning points:

- This case demonstrates how persistent uptake of tracer in a reactive submandibular lymph node can mimic an ectopic parathyroid adenoma.
- Incidental foci of increased tracer uptake may also be seen in other non-parathyroid entities such as a hyperplastic thymus or cervical, supraclavicular and axillary lymph nodes (normal and pathological). These findings may be incorrectly mistaken for parathyroid disease [3].
**Case 2:** A 75-year-old male presenting with PHPT. Blood tests showed an elevated adjusted Calcium of 3.09 mmol/L, PTH of 14.6 pmol/L and Phosphate of 0.61 mmol/L.

A parathyroid Tc99m Sestamibi was performed which demonstrated no abnormal persistent tracer uptake on the delayed images to suggest a parathyroid adenoma (Figure 3).

Subsequent explorative surgery failed to treat the primary hyperparathyroidism and a repeat sestamibi and SPECT was performed 1 year later (Figure 4). This was reported as demonstrating physiological tracer uptake and again no evidence of a parathyroid adenoma was identified.

Venous sampling however, revealed a high PTH at the left internal jugular vein and left thyro-cervical vein. Despite this, an USS of the neck did not demonstrate a convincing parathyroid adenoma.

A previously performed CT neck was reviewed retrospectively, which demonstrated a 12 x 13 mm enhancing nodule posterior to the internal carotid artery at the level of C1 (Figure 5). This was correlated to the previous Sestamibi scan which on reflection also demonstrated a focus of subtle tracer uptake in this region, suggestive of a possible parathyroid adenoma close to the skull base.

MRI neck with contrast was performed which showed an enhancing well-defined lesion (low T1 and intermediate T2 signal) on the left side of the neck posterior to the left internal carotid artery measuring 10 x 14 x 13 mm, corresponding to the nodule on the CT (Figure 6).

These findings were consistent with an ectopic parathyroid adenoma and surgical histology later confirmed a parathyroid adenoma in the left pharyngeal space.

**Learning points:**

- This case demonstrates an ectopic parathyroid adenoma diagnosed on CT/MRI with an initial false negative Sestamibi scan due to its location at the skull base.
- This case emphasises the importance of understanding the embryological development of the parathyroid glands and their normal migration pattern so that ectopic adenomas are not missed [3].
- The aberrant migration of parathyroid glands can include sites from the base of the jaw to the mediastinum [2].
**Case 3**: A 69-year-old female presented with PHPT. Blood investigations showed an adjusted Ca of 2.85 mmol/L, a PTH of 4.0 pmol/L and a Phosphate of 0.86 mmol/L.

A Tc99m Sestamibi was performed which demonstrated early uptake of tracer in the right lobe of the thyroid, which washed out on the delayed imaging (Figure 7). There was no persistent increased uptake to suggest a parathyroid adenoma.

Ultrasound of the neck failed to demonstrate a parathyroid adenoma.

A CT neck and thorax with contrast was subsequently performed which demonstrated a 10 x 15 mm area of enhancement posterior to the lower pole of the right lobe of thyroid (Figure 8). This corresponded to the focus of increased tracer uptake on the early images of the Sestamibi study.

Histology confirmed a parathyroid adenoma.

**Learning points:**
- This case demonstrates how a parathyroid adenoma can show early tracer uptake with atypical tracer wash out on delayed imaging and can result in false negative results, which have been attributed to differences in perfusion, metabolic activity and low mitochondrial content [4].

**Case 4**: A 78-year-old male presented with PHPT and a history of emphysema, lung adenocarcinoma and left lower lobectomy. Blood tests revealed an adjusted Ca of 2.71 mmol/l, PTH of 7.7 pmol/L and Phosphate of 0.50 mmol/l.

A Tc99m Sestamibi demonstrated a large focus of tracer accumulation within the mediastinum (Figure 9).

A CT neck and thorax was performed, which demonstrated an enhancing 45 mm lesion extending from the right paratracheal region into the precarinal region, which corresponded to the focal tracer accumulation seen on the Sestamibi scan (Figure 10).

Postsurgical histology confirmed metastatic adenocarcinoma.

**Learning points:**
• This case demonstrates a false-positive result where there was persistent increased uptake within the superior mediastinum on the Sestamibi scan, due to mediastinal adenopathy secondary to metastatic adenocarcinoma.
• Sarcoidosis and carcinoid tumours can also result in increased soft tissue tracer uptake in the thorax, which can make the evaluation of parathyroid disease much more challenging [3].
**Fig. 1:** Parathyroid Tc99m Sestamibi demonstrating asymmetrical tracer accumulation in the submandibular glands with increased uptake seen on the left (arrows); thought to represent either physiological uptake or an ectopic parathyroid. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2013.

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Fig. 2: Axial contrast CT section of the neck demonstrating an enhancing 8 x 10 mm nodule (arrow) anterior to the left submandibular gland corresponding to the focal tracer accumulation on the Sestamibi scan. Further smaller lesions are seen anterior and posterior to the left submandibular gland. Conclusion: Appearance are in keeping with prominent lymph nodes. The largest node accumulates Tc99m Sestamibi raising the possibility of malignancy. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2014.

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**Fig. 3:** Parathyroid Tc99m Sestamibi demonstrating no abnormal persistent tracer uptake on the delayed images to suggest a parathyroid adenoma. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2011.

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Fig. 4: Parathyroid Tc99m Sestamibi originally reported as demonstrating physiological tracer uptake and no evidence of a parathyroid adenoma. On reflection subtle persistent uptake of tracer is seen on the left side of the neck suggesting a possible parathyroid adenoma. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2012.

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**Fig. 5:** Axial and Coronal contrast CT sections of the head and neck (a,b) demonstrating a 12 x 13 mm enhancing nodule (arrows) posterior to the internal carotid artery at the level of C1 suggesting a possible parathyroid adenoma at the base of the skull. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2012.

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Fig. 6: Coronal T1 (a), coronal T2 fatsat (b), axial T1 post-contrast (c) and axial T1 (d) MRI sections of the head and neck demonstrating an enhancing well-defined lesion (arrows) on the left side of the neck posterior to the left internal carotid artery, measuring 10 x 14 x 13 mm. The lesion demonstrates low/intermediate signal on T1 (a,d) and intermediate signal on T2 (b). These findings are consistent with an ectopic parathyroid adenoma.

References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2012.

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Fig. 7: Parathyroid Tc99m Sestamibi demonstrates early uptake of tracer in the right lobe of the thyroid, which washes out on the delayed imaging. No persistent increased uptake to suggest a parathyroid adenoma. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2015.

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Fig. 8: Axial (a) and coronal (b) contrast CT sections of the neck and thorax demonstrating a 10 x 15 mm area of enhancement (arrow) posterior to the lower pole of the right lobe of thyroid. These findings are suggestive of a parathyroid adenoma. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2015.

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Fig. 9: Tc99m Sestamibi demonstrating a large focus of tracer accumulation within the mediastinum. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2014.

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Fig. 10: Axial (a) and Coronal (b) contrast CT sections of the neck and thorax demonstrate an enhancing 45 mm lesion extending from the right paratracheal region into the precarinal region. References: © Department of Radiology, Norfolk and Norwich University Hospitals NHS Foundation Trust, England 2014.

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Conclusion

Understanding the properties of Tc99m Sestamibi and the embryological, physiological and anatomical features of the parathyroid glands is essential to avoid misinterpretation of Tc99m Sestamibi scintigraphic studies.

Being aware of the common pitfalls of Tc99m Sestamibi scintigraphy therefore greatly enhances the accuracy of localising parathyroid adenomas, hence improving surgical outcomes [2].
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References


